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The therapeutic plan implementation in patients discharged from the hospital after myocardial infarction

According to the European Society of Cardiology guidelines dual antiplatelet therapy (DAPT) for 12 months, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), beta-blocker and statin [1] are recommended in patients after myocardial infarction (MI). Adherence to this treatment determines the achievement of therapeutic targets [2–8]. Previous studies have shown that patients after MI often do not adhere to the treatment plan. Discontinuation of the recommended post-MI therapy predisposes to serious thrombotic events, particularly MI, in-stent thrombosis, stroke and death [9–14]. The knowledge regarding the level and determinants of adherence to treatment recommendations in post-MI patients enables proper care and education planning for this population.

The series of recent publications reporting results of a single centre, observational, cohort clinical trial with 1-year follow-up, was intended to reflect 'real world' practice [15–18]. All study participants received in-hospital educational and motivational verbal interventions on ischemic heart disease, focusing on its symptoms and management supported by an educational brochure entitled "Myocardial infarction" that was handed out at the beginning of hospitalization. The first educational visit was carried out within the first two days after admission to the hospital. The visit included an assessment of patient knowledge of the disease, its symptoms, and prevention (20 standardized questions). Throughout the entire hospital stay, patients had an opportunity to ask questions and obtain comprehensive answers. The educational and motivational visits were conducted by trained educational nurses.

The readiness for discharge from the hospital was assessed using a validated questionnaire Readiness for Hospital Discharge after Myocardial Infarction Scale (RHD-MIS) [19, 20]. The RHDS-MIS consists of 23 questions included in three subscales assessing subjective (assessed by the patient) and objective (assessed by medical personnel) knowledge about the disease and patient expectations. Additionally, the questionnaire contains non-scored questions regarding the patient's opinion on the readiness for discharge.

The analysis of medication discontinuation was performed based on prescription filling data provided by the National Health Fund (NHF) for reimbursed drugs: ACEI (ramipril, perindopril) $P2Y_{12}$ receptor inhibitor (clopidogrel) and statin (atorvastatin, simvastatin, rosuvastatin). The NHF is the only institution in Poland that covers the costs of hospitalization, outpatient treatment and prescribed medications. Drugs non-reimbursed by the NHF were not included in the analysis. All study participants patients received appropriate prescriptions (including ACEI, $P2Y_{12}$ receptor inhibitor and statin) at discharge from the hospital. Two hundred fifty-two patients were enrolled on the study. The final analysis was conducted for 225 participants (73.3% men, 26.7% women) aged 30–91 years (mean age 62.9 ± 11.9 years), for whom data were obtained from the National Health Fund.

According to the authors' best knowledge, this research [15–18] is the first one to comprehensively

analyse the level of adherence to medication and its determinants as well as the variability of these determinants during the follow-up after hospital discharge.

The mean adherence level during 1-year of follow-up for all three groups of medications (ACEIs, P2Y$_{12}$ receptor inhibitors and statins) was 64.1 ± 24.5%, with a value of 67.2 ± 31.8% for ACEI, 61.6 ± 34.2% for P2Y12 receptor inhibitors, and 64.4 ± 32.1% for statins. Over time, a gradual decline in adherence was observed for all groups of medications. Sufficient adherence for all medication groups was found only in 29.4% of patients throughout the whole follow-up period [15–18]. These findings are in line with those obtained by Naderi et al. [2] in a meta-analysis of 20 studies evaluating 7 groups of drugs showing a mean adherence level of 57.0% and its decline over consecutive quarters of follow-up. Similar findings were reported also in other publications [11–14].

The multivariate analysis defined determinants of medication adherence: age under 65 years in the first quarter of follow-up for ACEI, P2Y12 receptor inhibitor and statin; prior CABG in the 1st quarter of follow up for ACEI and P2Y12 receptor inhibitor; level of education and place of residence for P2Y12 receptor inhibitor in the 1st quarter of follow-up; economic status for all assessed drugs in the 2nd quarter; marital status for ACEI in the 1st quarter of follow-up; arterial hypertension for ACEI in the 1st quarter of follow-up [15–18]. Identifying the factors responsible for the decline in adherence in the sequential quarters helps better understand the mechanisms governing this phenomenon and apply targeted corrective interventions. Additional educational and motivational efforts should be directed to elderly, less educated, living alone patients and those after CABG in order to increase the likelihood of implementation of prescribed medication after discharge from the hospital. Maintenance of medication during long term treatment requires special support in rural residents and patients with lower economic status [15–18].

The therapy discontinuation remains a challenge for therapeutic teams. Elimination of this phenomenon might largely improve the clinical and economical outcomes of treatment [3, 8, 16].

The highest likelihood of therapy discontinuation, including long-term discontinuation (> 30 days) and permanent therapy cessation was found for statins and the lowest for ACEIs. It was found that patients are most prone to discontinue therapy between the 2nd and 3rd quarter of follow-up. In contrast to the permanent cessation of therapy, a significant increase in the incidence of temporary therapy discontinuation was already seen in the 1st quarter of follow-up [15–18].

Multivariate logistic regression analysis identified occupational activity and a prior MI as independent predictors of lack of post-discharge therapy initiation with P2Y12 receptor inhibitors. The research found no predictors of lack of post-discharge therapy initiation with other medications either when analysed individually or together. Multivariate analysis indicated age above 65 years and prior revascularization as independent predictors of therapy discontinuation but failed to identify independent predictors of the permanent cessation of therapy with any of the medications as well as the temporary discontinuation and permanent cessation of treatment with all three medications together [15–18].

Preparation for discharge, including education in the field of secondary prevention after a MI, is a current standard of care, however, not always meeting the patient's expectations [21–27].

The assessment of readiness for discharge was based on the RHD-MIS. The analysis of adherence to treatment in relation to the results achieved in RHD MIS did not provide unequivocal results both in terms of the overall result and the results in individual subscales. This applies to individual drug groups tested separately and to all groups together. Significant differences noted in individual quarters for individual drugs may, contrary to expectations, suggest worse adherence in patients who were better prepared for discharge from the hospital [15–18]. These surprising results require further in-depth research to explain this phenomenon. According to the previously published studies, better adherence to treatment should be expected in patients with a higher level of readiness for discharge. The study confirms that patient education should continue after discharge from the hospital [26–36].

The patients with a high expectation score had longer treatment interruptions only for the P2Y12 receptor inhibitor. No relations between medication adherence and the level of expectations were found in the first two quarters, while for the last two-quarters of follow-up, however, an inverse relationship between the level of expectations and adherence was shown. When related to the levels of expectations (high vs medium vs low), adherence for ACEI in the 4th quarter of follow-up was 39 ± 31% *vs*. 58 ± 43% *vs*. 57 ± 43% (p = 0.0099; R = -0,16; p = 0.0187). Similarly, for P2Y12 inhibitor the numbers were 37 ± 41% *vs*. 53 ± 43% *vs*. 55 ± 41% (p = 0.0282; R = -0,15; p = 0.0438). No differences, however, were found for statins [15–18].

The observed relation of expectations and adherence might indicate a mismatch between the educational contents and patient expectations. The study protocol, however, did not include additional educational initiatives to be delivered to fulfil patient individual expectations after the provision of the standard education intervention. The identification of patient expectations might allow further personalization of educational and motivational programmes [15–18].

Several limitations of the research reported in the series of publications should be considered. Medications non-reimbursed by the National Health Fund

were excluded from the analysis. The authors analysed a limited number of factors as potential determinants of therapy discontinuation. Moreover, the authors do not have patients' reports concerning the reasons for therapy discontinuation. On the other hand, the strengths of this research are comprehensiveness and the homogeneity of the study population.

The reported research enabled making several important observations.

The vast majority of post-MI patients discontinue, either temporarily or permanently, one of the essential medications within one year following MI. Adherence to pharmacotherapy decreases over time after MI. Several socioeconomic and clinical factors have been identified to affect medication adherence over time. The readiness for discharge from the hospital assessed with the RHD-MIS does not clearly affect the implementation of the therapeutic plan in the long-term follow-up in patients after MI. Data suggesting a negative impact of some aspects of readiness for discharge on adherence to treatment require further, in-depth research.

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